AMENDMENTS TO THE CLAIMS:

1. (Currently Amended) A method of treating degeneration of the cartilaginoid matrix comprising administering to a subject in need thereof an effective amount of one or more compounds or <u>pharmaceutically acceptable</u> salts thereof having the following formula:

$$A-(B)_{b0}-(C)_{c0}-N(O)_{S}$$
 (I)

wherein:

s is an integer and is equal to 1 or 2;

c0 is an integer and is equal to 0 or 1;

b0 is an integer and is 0 or 1; with the proviso that at least one of c0 and b0 is different from zero;

 $A = R-T_{1-}$, wherein

R- is the radical of a non steroidal antiinflammatory precursor drug excluding the compounds having 2-oxo-1H-indolic structure, or the radical of a non steroidal antiinflammatory/analgesic drug;

 $T_1 = (CO)_t$ or $(X)_{t'}$, wherein $X = -O_{-}$, $-S_{-}$, $-N(R_{1C})_{-}$, R_{1C} is H or C_1 - C_5 linear or branched alkyl, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1;

 $B = -T_B - X_2 - T_{BI}$ - wherein

 T_B and T_{BI} are equal or different;

 T_B = (CO) when the reactive function in the precursor drug is -OH or -NH(R_{1C}); T_B = X, as above, when the reactive function in the precursor drug is -COOH;

 $T_{BI} = (CO)_{tx}$ or $(X)_{txx}$, wherein tx and txx have the value of 0 or 1; with the proviso that tx = 1 when txx = 0, tx = 0 when txx = 1; X is as above;

X₂ is a bivalent linking group as defined below;

C is the bivalent radical -T_c-Y- wherein

when b0 = c0 = 1: $T_C = (CO)$ when tx = 0, $T_C = X$ when txx = 0, X being as above;

when b0 = 0: $T_C = (CO)$ when t = 0, $T_C = X$ when t' = 0, X being as above; when c0 = 0: tx = 0, $T_{BI} = X = -O$ -;

Y is:

Y_p:

$$\begin{array}{c|cccc} R_{TIX} & R_{TIIX} \\ & & | \\ - & -[C]_{nIX} & - & Y^3 - [C]_{nIIX} - O - & (III^P) \\ & & & | \\ & R_{TIX'} & R_{TIIX'} \end{array}$$

wherein:

nIX is an integer from 0 to 10;

nIIX is an integer from 1 to 10;

 R_{TIX} , R_{TIX} , R_{TIIX} , R_{TIIX} , equal to or different from each other are H or C_1 - C_4 linear or branched alkyl;

Y³ is a saturated, unsaturated or aromatic heterocyclic ring containing one or two nitrogen atoms having 5 or 6 atoms,

or Y can be:

 Y_0 , selected from the following:

a –R'O– alkylenoxy group wherein R' is linear or branched when possible C₁-C₂₀, or a cycloalkylene having from 5 to 7 carbon atoms, in the cycloalkylene ring one or more carbon atoms can be substituted by heteroatoms, the ring can have side chains of R' type, R' being as above; or one of the following groups:

wherein nf' is an integer from 1 to 6;

wherein R_{1f} = H, CH₃ and nf is an integer from 1 to 6; or Y is Y_{Ar} and is selected from the following:

wherein n3 is an integer from 0 to 3 and n3' is an integer from 1 to 3;

wherein n3 and n3' have the above meaning;

- aminoacids,
- hydroxyacids,
- aromatic and heterocyclic mono- and [[polyalchols]] polyalcohols,
- compounds containing at least one free acid function.
- 2. (Withdrawn) The method of claim 1, wherein the precursor of B is selected from the following:
 - aminoacids selected from the following: L-carnosine (formula CI), anserine (CII), selenocysteine (CIII), selenomethionine (CIV), penicillamine (CV), N-acetylpenicillamine (CVI), cysteine (CVII), N-acetylcysteine (CVIII), glutathione (CIX) or esters thereof

(CI) (CII)

hydroxyacids, selected from the following: gallic acid (formula DI), ferulic acid
 (DII), gentisic acid (DIII), citric acid (DIV), caffeic acid (DV), dihydrocaffeic
 acid (DVI), p-cumaric acid (DVII), vanillic acid (DVIII):

aromatic and heterocyclic mono- and polyalcohols, selected from the following: nordihydroguaiaretic acid (EI), quercetin (EII), catekin (EIII), kaempferol (EIV), sulphurethyne (EV), hydroquinone (EVIII), gossypol (EIX), reductic acid (EX), methoxyhydroquinone (EXI), hydroxyhydroquinone (EXII), propyl gallate (EXIII), 3,5-di-ter-butyl-4-hydroxybenzyl-thioglycolate (EXXIV), allopurinol (EXXXI); saccharose (EC), ascorbic (ECI) and isoascorbic acid (ECII), p-cumaric alcohol (ECIII), 4-hydroxy-phenylethylalcohol (ECIV), coniferyl alcohol (ECV):

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compounds containing at least one free acid function, selected from the following: 3,3'-thiodipropionic acid (NI), fumaric acid (NII), dihydroxymaleic acid (NIII), edetic acid (NV):

- 3. (Previously Presented) The method of claim 1, wherein in the compounds of formula (I):
 - when b0 = c0 = 1, the bonds between the drug radical and X_2 and between X_2 and Y are, independently the one from the other, of ester, thioester, amide type; when b0 = 0 and c0 = 1 the bond between the drug radical and Y is of ester, thioester, amide type.
- 4. (Previously Presented) The method of claim 1, wherein the R radical is selected from the following groups:

Group I)

la)

$$R_2$$
 R_1

lb)

$$OCOR_{3OOO} O(R_{2})_{nl} (R_{1})_{nI}$$

wherein:

 R_1 is H or -OCOR₃; wherein R_3 is methyl, ethyl or C_3 - C_5 linear or branched alkyl, or the residue of an heterocycle with only one ring having 5 or 6 atoms partially or

totally hydrogenated, or aromatic, containing one or more heteroatoms independently selected from O, N and S;

 R_2 is hydrogen, hydroxy, halogen, C_1 - C_4 linear or branched alkyl, C_1 - C_4 linear or branched alkoxyl; a C_1 - C_4 linear or branched perfluoroalkyl; nitro, amino, monoor di- (C_{1-4}) alkylamino;

with the proviso that in formula Ia) R_1 and R_2 are not contemporaneously H; in formula Ib) nI is an integer 0 or 1;

Group II)

lla)

Ilb)

$$\begin{array}{c|c} & H_3C & CF_3 \\ \hline & N & \\ & H & \end{array}$$

wherein:

R_{II5} is H, C₁-C₃ linear or branched alkyl;

 R_{II6} has the same meaning as R_{II5} , or when R_{II5} is H it is benzyl;

 R_{II1} , R_{II2} and R_{II3} are independently hydrogen, C_1 - C_6 linear or branched alkyl, or C_1 - C_6 linear or branched alkoxy, or CI, F, Br;

R_{II4} is R_{II1} or bromine;

IIb) is the residue of the 2-[(2-methyl-3-(trifluoro methyl)phenyl]amino]-3-pyridincarboxylic] acid when T_1 = -CO- and the free valence is saturated with OH the compound is known as flunixin;

wherein:

 R_{2a} and R_{3a} are H, C_1 - C_{12} linear or branched, substituted or not, alkyl or allyl, with the proviso that when one of the two is allyl the other is H;

R_{1a} is selected from:

IIID) R_{1a} corresponds to the following formulas:

(XXXVII)

$$N \longrightarrow F$$
 $N \longrightarrow F$
 $N \longrightarrow F$

$$H_3C$$
 F
 CH_3
 C
 CH_3

wherein the meanings are the following:

- when R_{1a} is as defined in formula (IV), Ketoprofen residue: $R_{III1} \text{ is H, } SR_{III3} \text{ wherein } R_{III3} \text{ is } C_1\text{-}C_4 \text{ linear or branched alkyl;}$ $R_{III2} \text{ is H, hydroxy;}$
- when R_{1a} is as defined in formula (XXI), carprofen residue:

 R_{xxio} is H, alkyl from 1 to 6 C atoms linear or branched, C₁-C₆

 alkoxycarbonyl linked to a C₁-C₆ alkyl, C₁-C₆ carboxyalkyl, C₁-C₆ alkanoyl, optionally substituted with halogens, benzyl or halobenzyl, benzoyl or halobenzoyl;

 R_{xxi} is H, halogen, hydroxy, CN, C_1 - C_6 alkyl containing or not containing OH groups, C_1 - C_6 alkoxy, acetyl, benzyloxy, SR_{xxi2} wherein R_{xxi2} is C_1 - C_6 alkyl; C_1 - C_3 perfluoroalkyl; C_1 - C_6 carboxyalkyl containing or not containing OH groups, NO_2 , amino; sulphamoyl, di-alkyl sulphamoyl with C_1 - C_6 alkyl, or difluoroalkylsulphonyl with C_1 - C_3 alkyl;

 R_{xxi1} is halogen, CN, C_1 - C_6 alkyl containing one or more OH groups, C_1 - C_6 alkoxy, acetyl, acetamido, benzyloxy, SR_{III3} being R_{III3} as above, C_1 - C_3 perfluoroalkyl, hydroxy, C_1 - C_6 carboxyalkyl, NO_2 , amino, C_1 - C_6 mono- or di-alkyl-amino; sulphamoyl, C_1 - C_6 di-alkyl-sulphamoyl, or di-fluoroalkylsulphamoyl as above; or R_{xxi} together with R_{xxi1} is a C_1 - C_6 alkylen-dioxy;

- when R_{1a} is as defined in formula (XXXV) tiaprofenic acid residue:

 Ar is phenyl, hydroxyphenyl optionally mono- or polysubstituted with halogen, alkanoyl and C₁-C₆ alkoxy, C₁-C₆ trialkyl, cyclohexyl, cycloheptyl, heteroaryl, furyl containing or not containing OH, pyridyl;
- when R_{1a} is as defined in formula (II), suprofen residue, R_{3a} is H, R_{2a} is methyl and T_1 = -CO-;
- when R_{1a} is as defined in formula (VI), R is the residue of indoprofen when T_1 = -CO-, R_{2a} = H and R_{3a} = CH₃; of indobufen when R_{2a} is equal to H and R_{3a} = C₂H₅; T_1 = -CO-;
- when R_{1a} is as defined in formula (VIII), R is the etodolac residue when $R_{2a} = R_{3a} = H$ and $T_1 = -CO$ -;
- when R_{1a} is as defined in formula (VII), R is the fenoprofen residue when $R_{3a} = H$, $R_{2a} = CH_3$ and $T_1 = -CO$ -;
- when R_{1a} is as defined in formula (III), R is the fenbufen residue when R_{2a} = R_{3a} = H and T_1 = -CO-;
- when R_{1a} is as defined in formula (IX), R is the flurbiprofen residue when $R_{3a} = H$, $R_{2a} = CH_3$, $T_1 = -CO_7$;

- when R_{1a} is as defined in formula (X) R is the tolmetin residue when R_{2a} = R_{3a} = H, T_1 = -CO-.

In group IIID) R_{1a} corresponds to the following formulas:

- IIIa), when R_{2a} = H and R_{3a} = CH_3 the pranoprofen residue is obtained: α methyl-5H-[1]benzopyran-[2,3-b]pyridin-7-acetic acid;
- (XXX), when R_{2a} = H and R_{3a} = CH₃ the bermoprofen residue is obtained: dibenz[b,f]oxepin-2-acetic acid;
- (XXXI), when R_{2a} = H and R_{3a} = CH₃, R is the radical of the compound CS-670: 2-[4-(2-oxo-1-cyclohexyliden methyl) phenyl]propionic acid;
- (XXXII), when $R_{2a} = R_{3a} = H$, the pemedolac residue is obtained; when R_{2a} = $R_{3a} = H T_1 = -CO$ -;
- (XXXIII), when $R_{2a} = R_{3a} = H$, the pirazolac residue is obtained: 4-(4-chlorophenyl)-1-(4-fluorophenyl)-3-pyrazol acid derivatives;
- (XXXVI), when $R_{2a} = H$, $R_{3a} = CH_3$ the zaltoprofen residue is obtained; when the residue is saturated with an hydroxyl or aminic group, or with the carboxylic function the compounds are known as dibenzotiepin derivatives;
- (XXXVII), when $R_{2a} = R_{3a} = H$ the mofezolac residue is obtained: 3,4-di(p-methoxyphenyl)isoxazol-5-acetic acid when the residue is CH₂-COOH;
- (XII), when R_{2a} = R_{3a} = H the bromfenac residue is obtained: 2-amino-3-(4-bromobenzoyl)benzeneacetic acid;
- (XXXX) when $R_{2a} = R_{3a} = H$ the sulindac residue is obtained: (Z)-5-fluoro-2-methyl-1-[[4-(methyl sulphinyl) –phenyl]methylene]-1H-inden-3-acetic acid;

in Group IV) R is

wherein:

 R_{IVd} and R_{IVd1} are at least one H and the other an alkyl from C_1 to C_6 linear or branched, or difluoroalkyl with C₁-C₆ alkyl, or R_{IVd} and R_{IVd1} form together a methylene group;

R_{IV} has the following meaning;

wherein the compounds of group IV) have the following meanings:

in formula (IIB):

R_{iV-ii} is C₁-C₆ alkyl, C₃-C₇ cycloalkyl, C₁-C₇ alkoxymethyl, C₁-C₃ trifluoroalkyl, vinyl, ethynyl, halogen, C₁-C₆ alkoxy, difluoroalkoxy with C₁-

 C_7 alkyl, C_1 - C_7 alkoxymethyloxy, alkylthiomethyloxy with C_1 - C_7 alkyl, alkyl methylthio with C_1 - C_7 alkyl, cyano, difluoromethylthio, phenyl- or phenylalkyl substituted with the C_1 - C_8 alkyl; T_1 = -CO-;

- in formula (XB), of which the loxoprofen residue has been indicated, the compounds wherein R_{IVd} is H and R_{IVd1} is CH_3 ;
- in formula (IIIB):

 $R_{\text{iV-iii}}$ is a C_2 - C_5 branched or not branched alkyl, C_2 and C_3 alkyloxy, allyloxy, phenoxy, phenylthio, cycloalkyl from 5 to 7 C atoms, optionally substituted in position 1 by a C_1 - C_2 alkyl;

and R_{IVd} = H, R_{IVd1} is CH₃, compound known as ibuprofen residue, T_1 = - CO-;

Group V)

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$$(CH_2)_{2} = Rvii-1 O N N$$

$$Rvii$$

$$Rvii$$

$$Rvii$$

$$Rvii$$

Group VE)

$$\begin{array}{c|c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c|c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c}
CH_3
\end{array}$$

$$\begin{array}{c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c}
O & O \\
S & CH_3
\end{array}$$

$$\begin{array}{c}
O & O \\
S & CH_3
\end{array}$$

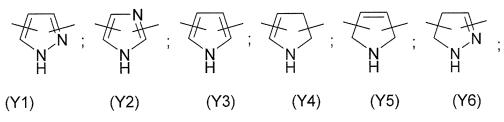
In group V), the compounds have the following meanings:

- when R is the formula (IIC),

R_{Vii} is H or a C₁-C₄ linear or branched alkyl;

 R_{Vii-1} is R_{Vii} , or C_1 - C_4 linear or branched alkoxy; CI, F, Br; the position of R_{Vii-1} being ortho, or meta, or para;

- when R is the formula (VIIC), of which the tenoxicam residue has been indicated, $T_1 = -0$ -;
- when R is the formula (IXC), wherein T_1 = -O-, the piroxicam residue has been indicated;
- when R is the formula (IIIC), wherein T_1 = -CO-, of which the nabumetone residue has been indicated;
- when R is the formula (IVC), wherein T_1 = -CO-, of which the indomethacin residue has been indicated;
- when R is the formula (XC), the residue X is known as meloxicam;
- when R is the formula (XI) the residue is known as ampiroxicam when the termination is -CH(CH₃)OCOC₂H₅;
- when R is the formula (XIII) and the valence is saturated with H, the residue derives from lornoxicam;
- when R is the formula (XXXXV), T_1 = -O- and the valence is saturated with H, the compound known as paracetamol is obtained.
- 5. (Withdrawn) The method of claim 1, wherein in the compounds of formula (I) Y³ of formula (III^P) of C is selected from the following bivalent radicals:



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- (Withdrawn) The method of claim 5, wherein Y³ is selected from the following:
 (Y12) with the two free valences in the ortho positions with respect to the nitrogen atom; (Y16) with the two valences linked to the two heteroatoms, Y1 (pyrazol)
 3,5-disubstituted.
- 7. (Currently Amended) The method of claim 1, wherein the compounds or pharmaceutically acceptable salts thereof of formula (I) are selected from the group consisting of:

2-acetyloxybenzoic acid 3-nitrooxymethyl phenyl ester (I^C);

2-fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 4-ni-trooxy butylester (II^C);

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-ni-trooxy butyl ester (III^C);

(S)-N-acetyl-[alpha-methyl-4-(2-methylpropyl)benzen-acetyl] cysteine 4-nitrooxybutylester having formula:

 $\hbox{4-nitrooxybutanoic acid 4-acetylaminophenylester (V^C);}\\$

trans-3-[4-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyloxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy) butyl ester, having formula:

$$(VI^{C})$$

2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 3-(ni-trooxymethyl)phenyl ester having formula:

$$\begin{array}{c|c} & & \text{CH}_3 \\ & & \text{ONO}_2 \\ & & & \\ & & \\ & & & \\ & \\ & & \\ & \\ & & \\ & \\ & \\ & & \\ & \\ & & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ & \\ &$$

(S)-N-acetyl-[2-fluoro-alpha-methyl(1,1'-biphenyl)-4-acetyl] cysteine 4-(nitrooxy)butyl ester having formula:

$$\begin{array}{c} \text{CH}_{3} & \text{NHCOCH}_{3} \\ \text{CH}_{2})_{4}^{2} \text{ONO}_{2} \\ \text{(VIII}^{\text{C}}) \end{array}$$

2-Fluoro-alpha-methyl[1,1'-biphenyl]-4-acetic acid 6-(nitrooxy methyl)-2-methylpyridyl ester having formula

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 4-(nitrooxy)butyl ester having formula :

MeO
$$(CH_2)_4$$
 ONO₂ $(CH_2)_4$ ONO₂

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 3-(nitrooxymethyl)phenyl ester having formula:

(S)-6-methoxy-alpha-methyl-2-naphthalenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl ester having formula:

$$(XII^{C})$$

trans-3-[4-[6-methoxy-alpha-methyl-2-naphthalenacetyl oxy]-3-methoxyphenyl]-2-propenoic acid 4-(nitrooxy)butyl ester having formula:

$$(XIII^{C})$$

(S,S)-N-acetyl-S-(6-methoxy-alpha-methyl-2-naphthaleneacetyl) cysteine 4-(nitrooxy)butyl ester having formula:

$$(XIV^{C})$$

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 4-(nitrooxy methyl)phenylmethyl ester having formula:

$$C1$$
 N
 ONO_2
 (XV^c)

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 6-(nitrooxymethyl)-2-methylpyridyl hydrochloride ester having formula:

(S)-3-benzoyl-alpha-methyl-benzenacetic acid 4-(nitro oxybutyl) ester having formula:

(S)-3-benzoyl-alpha-methyl-benzenacetic acid 3-(nitro oxypropyl) ester having formula:

$$(XVIII^{C})$$

(S)-3-benzoyl-alpha-methyl-benzenacetic 4-(nitro oxymethyl) phenylmethyl ester having formula:

5-benzoyl-2,3-dihydro-1H-pyrrolizine-1-carboxylic acid 4-(nitrooxy)butyl ester having formula:

$$(XXI^{C})$$

2-[(2,6-dichlorophenyl)amino]benzenacetic acid 5 (nitro oxy)ethyloxyethyl ester having formula:

$$C1$$
 $C1$
 $C1$
 (XX^C)

1-(4-Chlorobenzoyl)-5-methoxy-2-methyl-1H-indole-3-acetic acid 3-(nitrooxymethyl)phenyl ester (XXI^C).

- 8. (Currently Amended) The method of claim 1, wherein the compounds or pharmaceutically acceptable salts thereof of formula (I) are administered by oral, parenteral or topical administration.
- (Previously Presented) The method of claim 1, wherein relapses of degeneration of the cartilaginoid matrix in subjects in need thereof are reduced.